

Results from the Quality Research in Radiation Oncology (QRRO) survey: Evaluation of dosimetric outcomes for low-dose-rate prostate brachytherapy

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ABSTRACT

PURPOSE: We report on quality of dose delivery to target and normal tissues from low-dose-rate prostate brachytherapy using postimplantation dosimetric evaluations from a random sample of U.S. patients.

METHODS AND MATERIALS: Nonmetastatic prostate cancer patients treated with external beam radiotherapy or brachytherapy in 2007 were randomly sampled from radiation oncology facilities nationwide. Of 414 prostate cancer cases from 45 institutions, 86 received low-dose-rate brachytherapy. We collected the 30-day postimplantation CT images of these patients and 10 test cases from two other institutions. Scans were downloaded into a treatment planning system and prostate/rectal contours were redrawn. Dosimetric outcomes were reanalyzed and compared with calculated outcomes from treating institutions.

RESULTS: Median prostate volume was 33.4 cm³. Reevaluated median V_{100} , D_{90} , and V_{150} were 91.1% (range, 45.5–99.8%), 101.7% (range, 59.6–145.9%), and 53.9% (range, 15.7–88.4%), respectively. Low gland coverage included 27 patients (39%) with a D_{90} lower than 100% of the prescription dose (PD), 12 of whom (17% of the entire group) had a D_{90} lower than 80% of PD. There was no correlation between D_{90} coverage and prostate volume, number of seeds, or implanted activity. The median V_{100} for the rectum was 0.3 cm³ (range, 0–4.3 cm³). No outcome differences were observed according to the institutional strata. Concordance between reported and reevaluated D_{90} values (defined as within $\pm 10\%$) was observed in 44 of 69 cases.

CONCLUSIONS: Central review of postimplantation CT scans to assess the quality of prostate brachytherapy is feasible. Most patients achieved excellent dosimetric outcomes, yet 17% had less than optimal target coverage by the PD. There was concordance between submitted target-coverage parameters and central dosimetric review in 64% of implants. These findings will require further validation in a larger cohort of patients. © 2013 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords:

Prostate cancer; Brachytherapy; Quality assurance; Dosimetric outcomes

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Introduction

Prostate brachytherapy is widely practiced throughout the United States and is used as an effective first-line therapy for the management of patients with clinically localized prostate cancer. Postprocedure evaluation of the

quality of the implantation and the adequacy of the dose delivery to the prostate are routinely performed and considered standard of care. This quality assurance (QA) dosimetric assessment is based on the coordinates of the implanted seeds within the prostate gland as noted on a CT scan obtained 0–30 days after the procedure and accounts as well for the strength, number of the radioactive seeds, and their juxtaposition to the surrounding normal tissues. Dosimetric parameters measured include the radiation dose delivered to the prostate and the percentage of the prescription dose (PD) exposed to rectum and urethra.

There have been several single- and multiinstitutional series that have reported dosimetric outcomes after low-dose-rate permanent interstitial prostate brachytherapy (1–5). These reports have established expected standards of implantation quality; and, in a number of these reports, long-term tumor control outcomes have been linked to the adequacy of the dose delivery to the prostate based on the information obtained from this QA assessment (6–8). However, there is a paucity of information concerning the overall quality of implantation procedures as they are performed in various academic and nonacademic centers throughout the United States.

In an effort to obtain information regarding the overall quality of permanent seed implantation procedures as performed in the United States, Quality Research in Radiation Oncology (QRRO) performed a random survey of centers practicing prostate brachytherapy and obtained the postimplantation CT scans as well as dosimetric evaluations performed based on these scans. In a unique process, through a web-based remote deidentification process, postimplantation scans were downloaded to a central site from where they were extracted and underwent an independent evaluation by an expert institution. This report will summarize the dosimetric evaluation performed on these patients and compare these measures of quality to the dosimetric parameters submitted by the practicing institution.

Methods and materials

Of 414 eligible prostate cancer cases from 45 surveyed institutions, 86 patients received low-dose-rate brachytherapy and were eligible for this study. We collected CT images, dose distributions, and contours from 59 of the 86 patients from 15 of 21 institutions with eligible cases. Nineteen cases were not used owing to the inability to retrieve the images (i.e., images no longer available in the submitting institution's computer planning system, images stored in jpeg format only, or changes in software making it impossible for the site to transfer image data without updating software they no longer used); for eight cases, portions of data were missing that would have been needed to complete the dosimetric analysis. In addition, there were 10 test cases from two institutions that were initially used from a community institution (which was similar to the rest

of the sampled cohort) and were included to increase the number of cases evaluated for a final study cohort of 69 cases. Institutions in each of the four strata (academic, large nonacademic, medium nonacademic, and small nonacademic) participated.

Sample design

The QRRO survey used stratified two-stage cluster sampling, with radiation oncology facilities from a master list of those operating in the United States in 2007 being stratified, a random sample of facilities selected from each stratum, and a random sample of eligible cases selected from each participating facility. Facility strata were classified as academic (main teaching hospital of a medical school or National Cancer Institute-designated Comprehensive Cancer Center), large nonacademic (facility with at least three linear accelerators actively treating the patients), medium nonacademic (facility with two linear accelerators actively treating the patients), and small nonacademic (facility with one linear accelerator actively treating the patients). One hundred six facilities were selected and invited to participate in a survey of radiation therapy practices, of which 45 (42%) participated in the study: 14 academic, 13 large nonacademic, 7 medium nonacademic, and 11 small nonacademic facilities.

Case eligibility

Brachytherapy cases were randomly selected for review and data abstraction using lists of eligible patients provided by the treating facilities. Eligibility criteria for inclusion in the survey were as follows: (1) biopsy-proven adenocarcinoma of the prostate, (2) treatment that consisted of a permanent interstitial implantation, (3) treatment received during 1 year (2007), and (4) treatment in which the use of androgen-deprivation therapy in conjunction with radiotherapy was acceptable. Patients who had a prior radical prostatectomy or were treated for recurrent/metastatic disease were excluded. The characteristics of these patients as well as brachytherapy treatment details are summarized in [Tables 1 and 2](#).

Data collection

Trained research associates performed onsite reviews of the medical records of selected cases. Information about patient characteristics; tumor characteristics; staging workup; and brachytherapy treatment details, including isotope, seed strength, number of seeds, and PD, were collected and recorded in an online database.

Digital Imaging and Communications in Medicine CT images, contours of the prostate and rectum, and radiation dose files (which were extracted from a variety of treatment planning systems) were remotely deidentified and submitted from the sites to a control center at the Image-Guided Therapy QA center (ITC) located in St. Louis,

Table 1
Patient characteristics

Characteristics	Values
Age at start of RT	
Median (yr)	65
Range (yr)	49–83
Stratum	
Academic, <i>n</i> (%)	21 (36)
Nonacademic, <i>n</i> (%)	38 (64)
Prognostic risk group	
Favorable, <i>n</i> (%)	39 (66)
Intermediate, <i>n</i> (%)	17 (29)
Unfavorable, <i>n</i> (%)	2 (3.4)

RT = radiation therapy.

MO. The deidentified CT images were then uploaded from the ITC to a treatment planning system (Variseed Varian Brachytherapy, Charlottesville, VA) at the reference expert institution for this study (Memorial Sloan–Kettering Cancer Center) where the prostate and rectal anatomy were recontoured by one physician (LM) and checked carefully for accuracy by another (MJZ). Because these CT scans were obtained 2–6 weeks after the implantation procedure, a urinary catheter was not in place and delineation of the urethra for contouring purposes was not obtained.

Based on the new contours and the seed locations, dose–volume histograms were generated and dosimetric evaluation was performed for each of these cases. Dosimetric parameters analyzed included % V_{100} prostate (percent volume of the prostate that received the PD), D_{90} prostate (dose delivered to 90% of the prostate expressed in percent of the PD), % V_{150} prostate (percent volume of the prostate that received 150% of the PD), V_{100} rectum (percent volume of the rectum that received the PD), and D_{2cc} rectum (dose to 2 cc of the rectum expressed in percent of the PD).

For the purposes of comparing the newly generated dosimetric evaluation to the submitted evaluation from the treating institution, the new files were exported using Digital Imaging and Communications in Medicine protocol and uploaded to the ITC, where the files were registered to the originally submitted treatment evaluations. The spatial similarity between the submitted and reference expert prostate contours was assessed using a Dice's coefficient (9).

Table 2
Brachytherapy treatment details

Parameter	Number	Range
Median prostate volume (cc)	33	19–70
% V_{100}	91.1	46–100
% D_{90}	102	60–46
% V_{150}	54	16–88
Median V_{100} , rectum (cc)	0.3	0–4.3
Median D_{2cc} , rectum (%)	64	27–126

Results

Dosimetric outcomes based on evaluation of reference expert

The median prostate volume was 33.4 cm³ (range, 19.4–70.1 cm³). The median % V_{100} , % D_{90} , and % V_{150} were 91.1% (range, 45.5–99.8%), 101.7% (range, 59.6–145.9%), and 53.9% (range, 15.7–88.4%), respectively. Low gland coverage was observed in some patients: 27 (39%) were noted to have a D_{90} lower than 100% of PD; and of those, 12 (17%) had a D_{90} lower than 80% of the PD. For this data set, there was no correlation between D_{90} coverage and prostate volume, number of seeds, or total implanted activity. In addition, there were no apparent differences in D_{90} dose coverage according to the different institutional strata.

The median V_{100} for the rectum was 0.3 cc (range, 0–4.3 cc). The median D_{2cc} rectum doses were 64.3% (range, 27.3–126.1%). No differences were observed in terms of dosimetric outcomes according to the institutional strata.

Comparison of contours and dosimetric outcomes between submitted data and reference expert data

The Dice's coefficient was used to compare the submitted and reviewed prostate volumes, as shown in Fig. 1. The coefficient measures the intersection between the two volumes to be compared; thus a Dice's coefficient of 1 means that the two volumes can be superimposed and are equal. The average Dice's coefficient for the prostate volumes in these patients was 0.83 (range, 0.75–0.92) with a standard deviation (SD) of 0.04.

The median and SD of % D_{90} for the submitted and reviewed scans were 101.5% (SD, 17.6%) and 101.1% (SD, 18.5%), respectively (Fig. 2). We define D_{90} concordance to be good if the D_{90} value reported by the treating

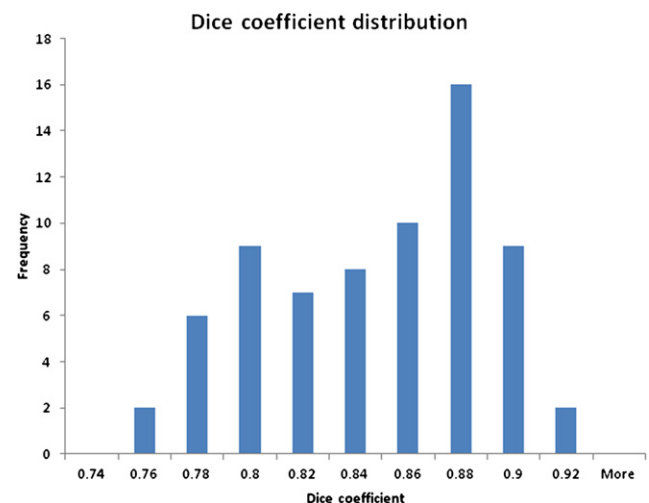


Fig. 1. Histogram of Dice's coefficient values indicating the spatial concordance of submitted and reviewed prostate volumes.

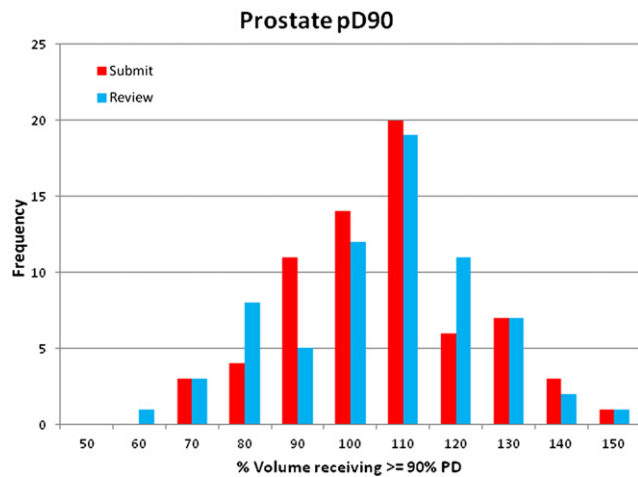


Fig. 2. Histogram of prostate pD₉₀ values (percent of prostate receiving 90% of PD) for submitted and reviewed plans. PD = prescription dose.

institution is within 10% of the reevaluated D_{90} . Good D_{90} concordance was observed in 44 of the 69 cases.

The median and SD of % V_{100} for the submitted and reviewed scans were 88.1% (SD, 10.7%) and 87.9% (SD, 11.2%), respectively. For the submitted contours and calculated doses, there were 32 patients (46%) with D_{90} lower than 100% of the PD and 18 patients (26%) with D_{90} lower than 90% of the PD. When these contours were centrally reviewed and doses were recalculated, 28 patients (41%) were noted to have a D_{90} lower than 100% of the PD and 17 patients (25%) had a D_{90} lower than 90% of the PD.

Figure 3 illustrates the similarities between the submitted and reviewer evaluations for % V_{150} . As demonstrated in Fig. 3, 4% and 7% of patients had V_{150} greater than 80%, suggestive of a “hot implant” based on the submitted and centrally reviewed dose calculations.

The average Dice’s coefficient for the rectal volumes in these patients was 0.8369 (range, 0.7533–0.9165) with an

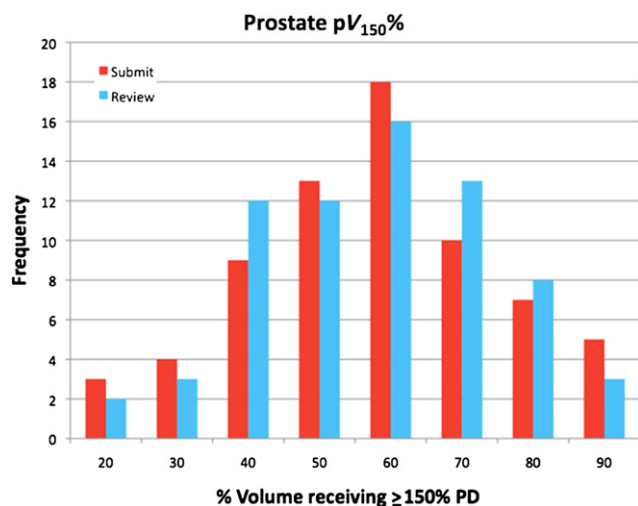


Fig. 3. Histogram of prostate pV₁₅₀ values (percent of prostate receiving greater than 150% PD) for submitted and reviewed plans. PD = prescription dose.

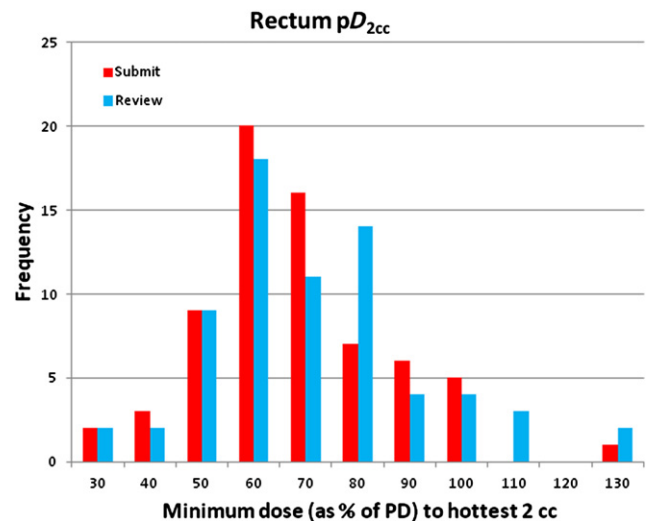


Fig. 4. Histogram of rectum pD_{2cc} values (percent of PD covering hottest 2 cc) for submitted and reviewed plans. PD = prescription dose.

SD of 0.0431. The median and SD of rectal D_{2cc} as a percentage of the PD was 62.7% (SD, 18.1) and 64.3% (SD, 20.3) for the submitted and reviewed scans, respectively (Fig. 4).

When all the above-mentioned analyses were performed excluding the 10 test cases, the findings were found to be not significantly different (data not shown).

Discussion

To our knowledge, this is the first report summarizing a concerted effort to evaluate the quality of prostate brachytherapy as part of a random survey of treating institutions within the United States. One of the primary objectives of QRRO is to assess the quality of care in radiation oncology as practiced in the United States. In 2007–2008, QRRO initiated a series of institutional surveys to evaluate the quality of treatment delivery for prostate, lung, cervix, and breast cancers based on the on-site evaluation of available treatment records. As the quality of prostate brachytherapy is essentially assessed primarily through the evaluation of the post-implantation CT scans, QRRO initiated an elaborate QA process to independently reevaluate the postimplantation scans and reanalyze the dosimetric parameters that are surrogates for quality and adequacy of the dose delivery to the prostate and normal tissues for patients treated with permanent interstitial implantation. In addition to reevaluation of the dosimetric parameters, this process would allow comparison of the submitted evaluation to the evaluation performed by an independent expert reviewer. Our report indicates that this QA evaluation is feasible and may serve as an opportunity for larger-scale QA assessments of individual institutions practicing prostate brachytherapy.

For this report, we evaluated brachytherapy quality of treatment delivery via a web-based remote deidentification program that facilitated scans being transferred to a central

depository (ITC) to allow external review from a single referee institution. The latter reevaluation process entailed recontouring and reassessing the dosimetric outcomes of the electronically transferred postimplantation CT scans. This exercise also afforded us the opportunity to compare dosimetric outcomes as submitted by the treating institution based on their internal QA review to that performed by the referee institution. The successful implementation of a central QA review has important implications not only for gauging the quality of brachytherapy as performed in the United States but also as a tool to provide external feedback and evaluate improvement of an individual's performance over time through serial assessments performed in a consistent fashion. Such a process has been used in the past for centralized review of eligibility of an institution; the presence of basic skills for performing implantation can be verified, to allow for institutional eligibility to enroll patients into prospective cooperative group studies (10). This process could be integrated in the future as part of self-assessment exercises for individual institutions to evaluate the quality of their procedures performed compared with other practicing centers.

Merrick *et al.* (11) have previously reported the dosimetric analysis of a large multiinstitutional database consisting of 6600 prostate implantation procedures performed by 129 brachytherapists from community practices. Implants were performed using a preplanned technique and the scans submitted to a commercial entity (Pro-Qura, Seattle, WA) for dosimetric analysis. The analysis technique used for these patients consisted of placing an inverted T on the preplan ultrasound and the corresponding postimplant CT axial image with the back of the T placed at the posterior aspect of the prostate. The ultrasound and CT images in this way were fused together to allow transfer of the volumes drawn initially on the preimplant ultrasound to be superimposed on the postimplantation CT scan. The authors defined "excellent" target coverage as V_{100} of 90% or greater and D_{90} of 100% or greater. Using these criteria, 48% of the implants were considered as having excellent dosimetry. In an earlier report (12), these authors defined a cohort of implants that were defined as "too cool" with V_{100} lower than 80% and/or D_{90} lower than 90%. Using these latter criteria, the percent of implant procedures that were "cool" and considered inadequate ranged from 13% to 36%.

The value of the postimplantation CT assessment is well recognized and considered the standard mode of postimplantation quality assessment. Several reports have indicated that the quality of the dose delivery to the prostate is associated with long-term biochemical tumor control. Stock *et al.* (2) had reported that D_{90} values lower than 140 Gy were associated with a higher incidence of prostate-specific antigen failure. A large multiinstitutional study demonstrated that D_{90} greater than 130 Gy was associated with an 8-year prostate-specific antigen relapse-free survival of 93% compared with 76% among patients who

had posttreatment D_{90} values lower than 130 Gy (7). Recently, investigators from Memorial Sloan–Kettering Cancer Center have shown that D_{90} greater than 140 Gy based on the dosimetric assessment of a postimplantation CT scan obtained on the day of the brachytherapy procedure predicted for improved long-term biochemical tumor control (5). Notwithstanding these findings, it is important to note that a dosimetric analysis indicative of suboptimal dose coverage will not necessarily result in an inferior tumor control outcome. Especially for patients with disease confined to a particular region within the prostate where the dose distribution happens to be adequate, tumor control would be expected despite what may be considered inadequate dose coverage for the rest of the gland. We acknowledge that there are limitations of the CT postimplantation assessment, which include postprocedure edema that can at times mistakenly characterize an implant as inadequate. Nevertheless, the postimplantation CT as a QA assessment is still considered standard of care after prostate brachytherapy and provides an opportunity for the radiation oncologist to perform a critical assessment of the inadequacies of target coverage. With greater awareness of the brachytherapist's target coverage and dose distributions achieved after the procedure, patterns of deficiencies can be potentially corrected with any necessary modifications of the technical aspects of the procedure.

The data presented in this report demonstrate acceptable quality outcomes based on dosimetric parameters assessed from the postimplantation scans and consistent with the finding of others (11–13). Although urethral dose assessments were not possible in the absence of a urinary catheter for anatomic visualization, the target coverage and rectal dose assessments indicate that implant procedures were generally performed well. Nevertheless, we observed that nearly 20% of evaluated cases had $\%V_{100}$ less than 80%, which we used as an indicator of suboptimal dose coverage of the prostate. Published reports of single-institutional dosimetric outcomes suggest that the percentage of cases with suboptimal dose coverage using this parameter ranges from 6% to 25% (14–23). We were not able to identify any patterns or predictors of suboptimal target coverage with the PD from particular institutions, or patterns within institutional strata (academic vs. nonacademic), number of implant procedures performed yearly, prostate size, or other patient-related characteristics. Our general impression in such cases of suboptimal coverage was that the seed location was predominately placed more inferiorly with resultant cold areas at the base and at times superior displacements with colder areas at the prostate apex. The incidence of higher rectal doses was noted in 13% of evaluated cases (Fig. 4) and no obvious predictors for higher rectal dosing were identified.

We recognize the limitations of this study, which include its retrospective nature and the relatively small cohort of postimplantation studies that were available for analysis. In addition, there are known uncertainties associated with the

exact delineation of target volumes from a CT scan used for postimplantation dosimetric analysis in particular at the prostatic base and apex as well as the anterior aspect of the gland with implanted seeds causing image artifact. Furthermore, we acknowledge that accuracy may have been further enhanced if multiple blinded observers would have been used to contour and recontour the images instead of as performed in this study with one investigator and along with a second physician to check for the accuracy of target delineation.

Our results nevertheless highlight the fact that not all implantation procedures will produce optimal dose delivery. In general, greater experience among practitioners has been shown to correlate with reduced incidence of poorly performed implant procedures. Yet we recognize that even with significant procedural experience, suboptimal target coverage with the PD can be observed even among the most experienced practitioners. Advances in real-time dosimetric evaluation and opportunities for accurate intraoperative corrections will likely contribute to further reductions in the likelihood of delivering suboptimal dosing to the gland and increase the odds of achieving greater consistency of dose delivery among practitioners.

Conclusion

In conclusion, we have demonstrated the feasibility of assessing the quality of prostate brachytherapy via remote independent review as part of a survey of practicing institutions in the United States. Our findings are consistent with optimal tumor coverage with the PD achieved in most of the treated patients. These data cannot be used to make broad generalizations regarding the adequacy of tumor coverage or quality of prostate brachytherapy procedures as performed in the United States, given the small sample size we analyzed. Yet it represents a study demonstrating the feasibility to assess the quality of implant procedures via a remote centrally located review. Such assessments provide an opportunity for self-assessment and will likely be used in the future as an important component for license recertification, as this process could be used to demonstrate proficiency of the practitioner.

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